

REMARKS/ARGUMENTS

Claims 1-9, 11-20, 22-26, 28,30 and 32-40 are pending.

Claims 1-4, 11-15, and 22-26 and 28 are currently under consideration.

Claims 5-9, 16-20, and 29-40 have been withdrawn as the result of an earlier restriction requirement.

In view of the examiner's earlier restriction requirement, applicant retains the right to present claims 5-9, 16-20, and 29-40 in a divisional application.

In response to the Office Action of November 21, 2006, Applicant requests re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

The Examiner's reconsideration of the previous restriction requirement is most appreciated.

Applicant's election with traverse of Group I, claims 1-28 and the species (A2) non-conjugated antibodies, (C6) antibody mediates cytotoxicity through production of a conformational change in a cellular protein effective to produce a signal to initiate cell-killing, and (D1) murine antibody has been acknowledged.

Applicants' argument that claims 33-40 do not recite the phrase "selected from the group consisting of . . ." and thus are not presented in a Markush format has been considered and was found persuasive.

Applicants' argument that the inventions of Groups I, III and IV have the same objectives, method steps and criteria for success has been considered, as has Applicants' argument that the treatment methods of Groups I, III and IV and the binding assay of Group II are each dependent upon the ability of the monoclonal antibody to interact with a MCSP antigenic moiety, and thus, Groups I-IV have the same criteria for success, i.e. the binding of the monoclonal antibody to a MCSP antigenic moiety.

Accordingly, it is most appreciated that the Examiner has indicated that Applicants' arguments have been carefully considered and are found persuasive, in part. Therefore Groups III and IV are rejoined because extending survival and delaying disease progression are overlapping criteria for success because delaying disease progression would be expected to extend survival.

It is understood that Groups I and Groups III/IV will remain separated for the reasons of record and additional reasons provided in the Office action.

Applicants' further argument that the non-conjugated and conjugated antibodies are not independent inventions since conjugation is a further limitation on the antibody has been given favorable consideration. Applicants' argument that conjugated antibodies comprise the same antibody as the non-conjugated antibodies (shared structure), which work by binding a MCSP antigenic moiety (shared mode of operation) to treat a cancerous disease (shared effects), and that a search for a non-conjugated antibody and the conjugated antibody clearly overlaps have also been considered.

Accordingly, the Examiner has indicated that upon review and reconsideration, given that the conjugation of antibodies to cytotoxicity enhancing compounds for enhanced efficacy in cancer treatment is well known in the art, the requirement for the election of species between an unconjugated and conjugated antibody will be vacated.

Applicants' argument that the types of conjugates (toxins, enzymes, radioactive compounds and hematogenous cells) are presented in a Markush format and that the restriction of a Markush group is proper only where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility has been considered, but has not been

found persuasive. The Examiner has taken the position that members of the Markush Group do not share a structural feature that is essential to their utility. The antibody is not a structural feature of each member of this group. The utility of these conjugates is in their toxicity and the structurally required features for this utility are clearly distinct for toxins, enzymes, radioactive compounds and hematogenous cells. Additionally different searches and issues are involved in the examination of each conjugate and the literature search is not coextensive. Thus, the restriction of the Markush group is deemed proper.

However, the Markush group of conjugates will be rejoined given that conjugated and unconjugated antibodies have been rejoined for examination and in the interest of facilitating prosecution.

Applicants have further argued that all six types of cytotoxicity mediated by the described antibody are not independent inventions because each type places a further limitation on the antibody by defining how the cytotoxicity of the antibody is achieved. Applicants argue that all six types have the same effect, i.e. cytotoxicity. Applicants argue that a search of the prior art should center on the specific monoclonal antibody. Applicants argue that one of skill in the art would

not attempt to search each of the six types of cytotoxicity mediated without connecting the search to the antibody since a search of the six types alone would result with thousands of hits related to many different antibodies. Applicants argue that the search for types of cytotoxicity is considered overlapping and thus, the election of species is improper. Applicants' argument has been considered, but the Examiner indicates that it has not been found persuasive because, for example, different antibody isotypes differ in their ability to stimulate complement-mediated cytotoxicity or antibody dependent cellular mediated cytotoxicity. Additionally, the Examiner posits that one of ordinary skill in the art would not predict that all antibodies, even those directed to the same antigen, would mediate all of the mechanisms of cytotoxicity claimed. The Examiner illustrates, by way of example, that not all antibodies have catalytic activity or can interfere with the function of the antigen they bind. Thus, he concludes that the antibodies that effectively mediate each of these forms of cytotoxicity are distinct, that the literature search is not coextensive, and thus different searches and issues are involved in the examination of each species.

Applicants further argue that there are no human antibodies disclosed; the antibodies disclosed in the instant

specification are murine antibodies and murine antibodies that have been humanized.

Upon review and reconsideration, the Examiner has acknowledged that the election of species between human and murine antibodies will be vacated.

The Examiner has indicated that the issues remain the same for the reasons set forth previously and above, thus the restriction requirement is deemed to be proper and is therefore made FINAL.

**Rejections under 35 USC 112 second paragraph**

Claims 1-4, 10, 11, and 23-28 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-4, 10, 11, and 23-28 are deemed to be indefinite by the Examiner because claims 1 and 23 recite the phrase "identifying characteristics".

Accordingly, the claims have now been amended to particularly recite "an isolated monoclonal antibody or antigen binding fragment thereof ... said antibody being an isolated monoclonal antibody or antigen binding fragment thereof which binds to the antigenic

moiety which is bound by the isolated monoclonal antibody produced by a hybridoma deposited with the ATCC as PTA-5643.

Thus, it is respectfully submitted that the metes and bounds of the claims have now been clarified and the rejection thereof has been overcome.

Claims 2, 4, 13, 15, 24, and 26 are indicated as being indefinite because they recite the phrase a "chimerized antibody". The Examiner indicates that the exact meaning of the word chimera is not known. The term chimera is generic to a class of antibodies which are products of genetic shuffling of antibody domains and other active proteins. The term encompasses antibodies fused to non-immunoglobulin proteins as well as antibodies wherein any domain of the antibody is substituted by corresponding regions or residues of human antibodies including but not limited to CDR grafted antibodies. Thus, it is the Examiner's position that the metes and bounds of the claim protection sought cannot be determined.

Accordingly, these claims have now been amended to recite "said isolated monoclonal antibody or antigen binding fragments thereof is a humanized or chimeric antibody of the isolated monoclonal antibody produced by the hybridoma deposited with the ATCC under accession number PTA-5643".

It is respectfully submitted that the metes and bounds of the claims are now defined and that the rejection thereof has been overcome.

Claims 1-4, 10-15, 21 and 22 are indicated as being indefinite because claims 1 and 12 recite the phrase "essentially benign". The claims are indefinite because the specification provides no definition of "essentially benign". Thus it is not possible to determine what essentially benign is.

Accordingly, the claims have been amended to delete the objected to phraseology "essentially benign".

Claim 28 recites the limitation "humor tumor tissue sample" in claim 23. There is alleged to be insufficient antecedent basis for this limitation in the claim.

Accordingly, the claim has been modified to obviate this rejection.

**Rejections under 35 USC 112 first paragraph:**

Claims 23-29 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which the Examiner alleges was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a process for mediating cytotoxicity of a human tumor cell which expresses an MCSP antigenic moiety on the cell surface comprising: contacting said tumor cell with an isolated monoclonal antibody or antigen binding fragment thereof, said antibody or antigen binding fragment thereof being an isolated monoclonal antibody or antigen binding fragment thereof which binds to said expressed MCSP antigenic moiety, said antigenic moiety characterized as being bound by an antibody having the identifying characteristics of a monoclonal antibody encoded by the clone deposited with the ATCC as PTA-5643, whereby cell cytotoxicity occurs as a result of said binding.

As illustrated *supra*, it is respectfully submitted that the claims have now been modified to set the metes and bounds thereof, and thereby obviate this ground of rejection.

Claims 10 and 21 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 10 and 21 have been canceled without prejudice to the subject matter contained therein.

Claims 1-4, 10-15, and 21-27 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a **breast or ovarian cancer** or for mediating cytotoxicity of **a breast or ovarian tumor cell** with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-5643, does not reasonably provide enablement for a method for treating a patient suffering from **a cancerous disease** or for mediating cytotoxicity of **a human tumor cell** with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-5643. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims have been amended accordingly to be limited to breast or ovarian tumor cells or cancerous disease, thereby obviating this ground of rejection.

Claims 1-4, 10, 11 and 23-28 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a cancerous disease or for a process for mediating

cytotoxicity with a monoclonal antibody or antigen binding fragment encoded by the cloned deposited with the ATCC as PTA-5643, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody or antigen binding fragment **having the identifying characteristics** of a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-5643. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims have been amended to remove the objected to language and are limited to an isolated monoclonal antibody or antigen binding fragment thereof which binds to the antigenic moiety which is bound by the isolated monoclonal antibody produced by a hybridoma deposited with the ATCC as PTA-5643.

It is respectfully submitted that the instant ground of rejection is obviated by this amendment to the claims.

Claims 1, 3, 10-12, 14, 21, 23, 25, and 27 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a cancerous disease or for a process for

mediating cytotoxicity with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-5643, wherein said antibody is a **humanized** antibody, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody having the identifying characteristics of a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-5643, wherein said antibody is a **murine** antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims read on treating a human tumor in a mammal with a mouse monoclonal antibody PTA-5643. This means the claims read on, and the specification contemplates, the treatment of cancer in humans with antibodies produced in a mouse.

It is respectfully submitted that numerous patents teach the real-world utility of treating a tumor cell with a murine antibody.

The fact that a HAMA response might emanate (the occurrence of a HAMA response is not an absolute) as a result of such treatment does not detract from the inherent real-world utility which has been demonstrated.

It is therefore requested that this ground of rejection be withdrawn.

Claims 3, 4, 14, 15, 25 and 26 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method for treating a patient suffering form a cancerous disease in accordance with claims 1 and/or 12 or a process for mediating cytotoxicity of a human tumor cell which expresses an MCSP antigenic moiety on the cell surface with antibody or antigen binding fragment there of having the identifying characteristics of a monoclonal antibody encoded by a clone deposited with the ATCC as PTA-5643, wherein said isolated antibody or antigen binding fragments thereof are conjugated with a member selected from the group consisting of cytotoxic moieties, **cytotoxic enzymes**, radioactive compounds, and hematogenous cells, whereby an antibody conjugate is formed does not reasonably provide enablement for the method for treating a patient suffering form a cancerous disease in accordance with claims 1 and/or 12 or a process for mediating cytotoxicity of a human tumor cell which expresses an MCSP antigenic moiety on the cell surface with antibody or antigen binding fragment there of having the identifying characteristics of a monoclonal antibody encoded by a clone deposited with the ATCC as PTA-5643, wherein said isolated

antibody or antigen binding fragments thereof are conjugated with a member selected from the group consisting of cytotoxic moieties, **enzymes**, radioactive compounds, and hematogenous cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims have been amended to obviate this ground of rejection.

Claims 1-4, 10, 11 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 10, 11 and 23-28 are broadly drawn to a method for treating a patient suffering from a cancerous of a disease or to a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody or antigen binding fragment **having the identifying characteristics** monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-5643.

The claims have been amended to obviate this ground of rejection.

**Claim Rejections - 35 USC § 102:**

Claims 23, 25, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Bumol et al. (PNAS, 1983, 80:529-533, IDS item).

The claims have been amended to obviate this ground of rejection.

**Claim Rejections - 35 USC § 103:**

Claims 1-4, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bumol et al. (PNAS, 1983, 80:529-533, IDS item) as applied to claims 23, 25, and 27 above, in further view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), in further view of Miller and Tannock (The Basic Science of Oncology, 2<sup>nd</sup> ed., McGraw- Hill Inc., 1992, Ch.14), and in further view of Riechmann et al (Nature Vol 332:323-327 1988).

The claims have been amended to obviate this ground of rejection.

**Double Patenting**

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefore ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-4, 10-15, and 21-27 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-4, 10-15, and 21-27 of copending application 10/949,846.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-4, 10-15, and 21-27 of copending application 10/949,846 will be cancelled in order to obviate this ground of rejection.

Likewise claims 29 and 31 of this application are cancelled to obviate the double patenting rejection made in S.N. 10/949,846.

Claim 28 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28 of copending Application No. 10/949,846.

Claims 1-4, 12-15, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-12, 15, 16 and 18 of copending Application No. 10/892,597.

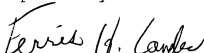
Claims 1-4, 12-15, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-10 of copending Application No. 11/370,255.

Terminal Disclaimers are filed concurrently herewith in order to obviate these grounds of rejection.

SUMMARY

In light of the foregoing remarks and amendment to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



Ferris H. Lander  
Registration # 43,377

McHale & Slavin, P.A.  
2855 PGA Boulevard  
Palm Beach Gardens, FL 33410  
(561) 625-6575 (Voice)  
(561) 625-6572 (Fax)